REMARKS

This response addresses the Office Action dated, May 15, 2007. Currently, claims 1-17 and 25 stand rejected.

I. Sequence Compliance

The Examiner has raised a rejection based on failure to comply with the Sequence Listing rules of 37 C.F.R. 1.821. Applicant notes that a paper copy of the Sequence Listing and Computer Readable Form (CRF) of the Sequence Listing were submitted on April 15, 2004. The Sequence Listing and CRF were is compliance with the rules in effect at the time of filing.

The Examiner's objection with regard to claim 5 is moot based on the present amendment. Therefore, the Applicant respectfully requests that the Examiner withdraw this objection.

II. Claim Objections

The Examiner has objected to claims 1 and 25 based on a formatting formality. By the present Amendment the claims have been reformatted. Therefore, the Applicant respectfully requests that the Examiner withdraw this objection.

III. Claim Rejections

1. 35 U.S.C. § 112, First Paragraph

The Examiner has rejected claims 1-17 and 25 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner states that one of skill in the art would not recognize from the disclosure that applicant was in possession of the genus which comprises the genus of derivatives of the carrier and the linker. The Examiner appears to suggest that only a single embodiment is disclosed; "i.e., wherein the peptide is Tyr-Gly-Gly-Phe-Met, carrier is a cinnamoyl, and wherein the linker is -C6 or C8 acidic moiety." (page 6 of Office Communication).

The analysis of whether the specification complies with the written description requirement is conducted from the standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art. Wang Labs. v. Toshiba Corp., 993 F.2d 858, 865 (Fed. Cir. 1993). Generally, the more sophisticated that a person of skill in the art would be, the less disclosure necessary to satisfy the written description requirement. As previously stated, the Federal Circuit has held that "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met … even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006) (emphasis added).

The Examiner concedes that the level of skill in the art pertaining to the present invention is high "with regard to conception, synthesis, and experimental protocols and data analysis of experimental results." (page 4 of Office Communication). Therefore, as previously indicated, the more sophisticated that a person of skill in the art would be, the less disclosure necessary to satisfy the written description requirement. *See* Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80 (Fed. Cir. 1986) (every nuance of the claims need not be explicitly described in the specification to satisfy the description requirement of section 112).

The Examiner's statement that only a "single species of the claimed genus" is disclosed is erroneous. The specification discloses that the peptide can be any therapeutic peptide having less than or equal to 40 amino acid residues. *See* paragraph [0011]. The Specification also discloses that the carrier moiety can be any one of either a finite set of chemical species or derivatives thereof. *See* paragraph [0013]. Moreover, the specification discloses that the linker may also be selected from a discrete set of chemical species that includes C6 to C16 lipidic chains, a 8-amino-3,6-dioxaoctanoic acid and polymers thereof, a natural peptide, a pseudopeptide of less than 4 residues, a peptide mimic of less than 4 residues and combinations thereof. *See* paragraph [0015] and [0018]. As such, the specification adequately describes the entire genus such that a person of skill in the art would appreciate that the Applicants were in possession of the entire scope of the claims at the time of filing the instant application.

It is axiomatic that an Applicant need not provide and example of every embodiment within the scope of the claims in order to satisfy the written description requirement (i.e., an inventor may submit prophetic examples). The Federal Circuit has long held that a claim's scope does not run afoul of section 112 simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. *See* Union Oil Co. v. Atl. Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000). It appears that the Examiner, is improperly attempting to limit the scope of the claims based on the description of certain preferred embodiments. *See* Specialty Composites v. Cabot Corp., 845 F.2d 981, 987 (Fed. Cir. 1988) ("particular embodiments appearing in the specification will not generally be read into the claims…What is patented is not restricted to the examples, but is defined by the words in the claims."); and Intervet Am., Inc. v. Kee–Vet Labs., Inc., 887 F.2d 1050, 1053 (Fed.Cir.1989) (the claims are not generally limited by specific examples appearing in the specification).

The Examiner states that the specification does not describe sufficient structure or physical/chemical properties of the carrier or linker molecules in order for a person of skill in the art to understand that the inventors were in possession of the entire scope of the claims. On the contrary, the present invention describes the use of a limited number of chemical moieties useful as a carrier in the composition of the invention. Specifically, the specification teaches that "the carrier comprises an aryl or alkyl group of sufficient length and/or steric bulk to inhibit rapid enzymatic degradation of the active drug species in vivo." *See* paragraph [0022]. The genus of possible chemical moieties is further limited through the recitation of specific groups selected from "a cinnamoyl, a benzoyl, a phenylacetyl, a 3-OH-cinnamoyl, a 3,4-OH-cinnamoyl, a 3,4-methylenedioxycinnamoyl, a 3-methoxycinnamoyl, a 3,4-dimethoxycinnamoyl, a 3,4,5-trimethoxy-cinnamoyl, a *t*-butoxy-carbonyl, a benzyloxycarbonyl, a pivaloyl, a N-9-fluorenylethoxycarbonyl, a fumaroyl…" and derivatives thereof. See paragraph [0022]. Therefore, a person of skill in the art would appreciate that the important structural feature shared by these specific compounds is the presence of steric bulk, and an aryl or alkyl group of sufficient length. As indicated above, there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure." Falkner v. Inglis, 448 F.3d 1357, 1366 (Fed. Cir. 2006). This is especially true where, as here, the chemical moieties are well known and there structural similarities would be obvious

to a person of skill in the art. For example, Table 1 presents the structure of a representative member of each subgenus of carrier moiety. As one of skill in the art would recognize, each member contains an aryl or substituted alkyl, and a carbonyl group.

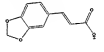
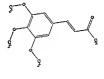
TABLE 1

Subgenus Chemical Moiety	Exemplary Structure
Benzoyl	
Cinnamoyl	
Phenylacetyl	
Benzyloxycarbonyl	
t-butoxycarbonyl	
Pivaloyl	
Fumaroyl	

As previously stated, the term "derivative," as used in the present specification is intended to carry its plain and ordinary meaning which is widely understood by those of skill in the art as a compound derived or obtained from another and containing essential elements of the

parent substance. *See* Abraxis Bioscience v. Mayne Pharma, 467 F.3d 1370, 1376 (Fed. Cir. 2006) (derivatives defined as compounds synthesized from a lead compound by one or more chemical reactions). As such, a person or ordinary skill in the art reading the present specification would understand that the derivatives, as presently claimed, also require the presence of the same structural hallmarks. For example, the specification expressly teaches the use of two derivatives of cinnamoyl in the composition of the invention: 3,4,5-trimethoxy-cinnamoyl, and 3,4-methylenedioxycinnamoyl (Table 2), which comprise the structural hallmarks described above.

TABLE 2

Cinnamoyl Derivative	Exemplary Structure
3,4-methylenedioxycinnamoyl	
3,4,5-trimethoxy-cinnamoyl	

Moreover, the specification teaches that the functional effect of having these particular carrier moieties linked to a peptide drug is the "significantly improved pharmacological and therapeutic effects for the active drug moiety…to enhance the absorption and bioavailability of an active peptide drug substance….[and] increasing thereby the in vivo half-life of the therapeutic component and improving its pharmacological properties." See paragraphs [0005], [0020], and [0025]. Therefore, the specification contains sufficient teaching of carrier structure, physical and chemical properties, and functional characteristics such that a person of skill in the art would appreciate that the inventors had possession of the entire scope of the claims.

Similarly, the specification teaches that various chemical moieties can be used as a linker in the drug composition of the invention, including peptides, pseudopeptides, and peptide mimics ([006], [0015]), and C6-C16 lipids ([0011], [0017], [0044], and Example 2). Specific examples taught and described in the specification include, in addition to 8-amino-3,6-dioxaoctanoic acid,

the use of palmitoyl ([0044]), aminooctanoyl ([0044]), hydroxyvaleryl-aminoactanoyl ([0044]), and psudedopeptides, for example, Gly-carba-Gly ([0044]). As discussed above, a person of ordinary skill in the art would be able to appreciate what is encompassed by the claims, and would understand that the inventors were in possession of the entire scope of the claim at the time of filing. *See* Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1379-80 (Fed. Cir. 1986) (adequate description requirement is met if a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification).

Therefore, Applicant maintains that the specification provides adequate disclosure to allow persons of ordinary skill in the art to recognize that Applicants were in possession of the entire scope of what is claimed. Notwithstanding the above, the Applicant has amended the claims for simplicity and clarity. As such, the Applicant respectfully requests that the Examiner withdraw this grounds for rejection.

2. 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-4 and 25 under 35 U.S.C. § 102(b) as being anticipated by Bodor (USPN 5,624,894). Specifically, the Examiner states that Bodor discloses novel peptide derivatives which are designed to deliver active peptides (2-20 aa in length) into the CNS. The Examiner states that the peptides are modified by linking a DHP-type redox moiety via an amino acid linker, and that Bodor also discloses that acyl group such as benzoyl and phenylacetyl are used to protect OH- groups during synthesis and/or to improve lipoidal characteristics and to prevent premature metabolism of the OH- groups prior to the compound reaching the desired site in the body.

In order to anticipate a claim under 35 U.S.C. §102, all of the limitations of the claim must be disclosed in a single prior art reference. MPEP § 2131; Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631 (Fed. Cir. 1987); Lewmar Marine Inc. v. Barient, Inc., 827 F.2d 744, 747 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 1007 (1988). Moreover, the single source must disclose all of the claimed elements "*arranged as in the claim.*" Structural Rubber Prods. Co. v. Park Rubber Co., 749 F.2d 707, 716 (Fed. Cir. 1984). In addition, the disclosure in an

assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research, 346 F.3d 1051, 1054 (Fed. Cir. 2003).

Bodor fails not only to teach every element of the claimed invention but also fails to teach every element "arranged as in the claim" of the present application. The instant claims are drawn to a peptide-derived therapeutic having a specific structure comprising, in order: a **carrier moiety**, selected from the group consisting of cinnamoyl, benzoyl, phenylacetyl, 3-OH-cinnamoyl, 3,4-OH-cinnamoyl, 3,4-methylenedioxycinnamoyl, 3-methoxycinnamoyl, 3,4-dimethoxycinnamoyl, 3,4,5-trimethoxy-cinnamoyl, *t*-butoxy-carbonyl, benzyloxycarbonyl, pivaloyl, N-9-fluorenylethoxycarbonyl, fumaroyl and derivatives thereof; a **linker** species consisting of C6 to C16 lipidic chains, 8-amino-3,6-dioxaoctanoic acid, natural peptides, pseudopeptides of less than 4 residues, peptide mimics of less than 4 residues, derivatives, and combinations thereof; and a peptide having from 1 to 40 amino acids. The present specification expressly teaches that one of the advantage of the claimed structure is that it is resistant to enzymatic digestion, and therefore, increases the in vivo half-life and overall bioavailability of the peptide therapeutic.

Bodor shows a therapeutic construct designed to address the unique biophysical challenges associated with getting a peptide therapeutic across the blood-brain barrier. Transport of solutes across the blood-brain barrier is notoriously difficult and requires the use of an approach that renders the construct unsuitable for systemic uptake of a therapeutic. For example, the therapeutic construct of the instant claims is designed specifically to be resistant to protease degradation while still being efficacious.

In stark contrast, the therapeutic of Bodor is designed for the "delivery of pharmacologically active peptides by sequential metabolism." (Col. 14, lines 54-55). In particular, Bodor teaches that the DHP moiety is essential in mediating delivery of the therapeutic peptide across the physical and enzymatic blood-brain barrier. (Col. 14, lines 60-65). In addition, the "spacer" moiety, which Bodor teaches as a peptide, must be a peptide so that it allows enzymatic cleavage and release of the "packaged" peptide. Furthermore, Bodor teaches the use of certain chemical moieties as protecting groups on the carboxy-terminus of the

therapeutic peptide to protect against degradation of the c-terminal amino acids. Neither the protecting groups nor their use as taught by Bodor is novel. However, Bodor teaches the use of certain protecting groups on the c-terminus hydroxyl group of a therapeutic peptide to prevent enzymatic degradation of the c-terminus.

Bodor does not teach or describe nor does it enable the use of cinnamoyl, benzoyl, phenylacetyl, 3-OH-cinnamoyl, 3,4-OH-cinnamoyl, 3,4-methylenedioxycinnamoyl, 3-methoxycinnamoyl, 3,4-dimethoxycinnamoyl, 3,4,5-trimethoxy-cinnamoyl, *t*-butoxy-carbonyl, benzyloxycarbonyl, pivaloyl, N-9-fluorenylethoxycarbonyl, fumaroyl and derivatives thereof, as a CARRIER moiety conjugated to a linker moiety. The only chemical moiety taught in Bodor that could possibly be construed as a carrier-type of moiety is the dihydropyridine moiety, which is not recited in the instant claims. As such, Bodor fails to disclose all of the claimed elements as arranged in the instant claims. *See* Structural Rubber Prods. Co. v. Park Rubber Co., 749 F.2d 707, 716 (Fed. Cir. 1984).

Moreover, Bodor expressly teaches that the use of a protecting group on the amino terminus would be useless because it would result in enzymatic degradation of the carboxy terminus of the therapeutic peptide. In stark comparison, the present invention teaches that the carrier moiety conjugated to a linker on the amino terminus of the therapeutic peptide is sufficient to reduce the enzymatic degradation of the therapeutic peptide.

Therefore, Bodor fails to anticipate the present invention under 102(b) because it does not teach, suggest, or enable the claimed arrangement of the specific carrier moieties conjugated to the specific linker species, which is bound to the amino terminus of a peptide. Furthermore, Bodor does not enable the claimed combination for improved bioavailability or enhanced pharmacologic properties for systemic drug uptake. As such, Bodor does not anticipate the present invention and is not a proper 102(b) reference.

In view of the comments presented above, Applicant believes that this grounds for rejection has been adequately traversed. Therefore, Applicant respectfully requests that Examiner withdrawn this grounds of rejection.

Because the reasons above are sufficient to traverse the rejection, Applicants have not explored, nor do they now present, other possible reasons for traversing such rejections.

Nonetheless, Applicants expressly reserve the right to do so, if appropriate, in response to any future Office Action.

IV. Obviousness Type Double Patenting

The Examiner has rejected claims 1-17 and 25 on the grounds of obviousness type double patenting in view of claims 1, 3, 7, and 9-14 of U.S. Patent No. 6,908,900 to Zimmer.

At the time of invention the instant claims and those of USPN 6,908,900 were commonly owned by Zimmer & Associates AG (currently d/b/a ImmuPharma SA), and commonly assigned. Therefore, the present rejection can be overcome through the submission of a terminal disclaimer, filed herewith.

Applicant believes that this grounds for rejection has been adequately traversed. Therefore, Applicant respectfully requests that Examiner withdrawn this grounds of rejection.

CONCLUSION

Applicant honestly believes that all aspects of the present Office Action have been sufficiently addressed and submits that the present application is now in condition for allowance, and notice to that effect is respectfully requested.

If the Examiner believes that a telephone conference with Applicants' attorneys would be advantageous to the disposition of this case, the Examiner is cordially requested to telephone the undersigned. If the Examiner has any questions in connection with this paper, or otherwise if it would facilitate the examination of this application, please call the undersigned at the telephone number below.

Authorization is hereby given to charge the $65.00 fee for Terminal Disclaimer for Small Entity to Deposit Account 50-3569. If any additional fee is required, please consider this a petition therefore, or otherwise if necessary to cover any deficiency in fees already paid, authorization is hereby given to charge our Deposit Account No. 50-3569.

Respectfully submitted,

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